Original Article

Prevalence of Peripheral Arterial Disease in Middle Aged (40 years and above) Diabetic Patients and Its Correlation with Carotid Intima-media Thickness in North 24 Parganas District Hospital

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Background : Diabetes Mellitus (DM) is an independent risk-factor of coronary artery disease (CAD). Over thirty million people have been diagnosed with diabetes in India (Diabetes.co.uk). The CPR (Crude Prevalence Rate) in the urban and rural areas in India are approximately 9% and 3% of the total population respectively. North 24 Parganas District of West Bengal is one of the most populated Districts of India (second only to Thane District of Maharashtra). As per 2011 census, the population of North 24 Parganas approximates about one crore (rural 4275724 and urban 5807128). In spite of the high disease burden (as per national average of Diabetes Mellitus), very few studies have been conducted till now regarding the diabetic population of North 24 Parganas, West Bengal.

Methods : A descriptive cross-sectional study has been conducted in North 24 Parganas District Hospital, Barasat, to find out the prevalence of peripheral arterial disease (PAD) by ankle-brachial index (ABI), in middle aged(40 years and above) diabetic patients and to find out the correlation with carotid intima-media thickness (CIMT), as they often co-exist with coronary artery disease (CAD), cerebrovascular disease or other complications of Diabetes Mellitus.

Results : Coronary atherosclerosis is often clinically silent with serious morbidity and mortality at its first presentation. In the present study, the mean age was 53.87 years, mean duration of DM was 6.76±5.78 years, with 70% of patients having abnormal ABI values (=0.9) and 46% of patients having abnormal CIMT (>0.8). They were correlated with each other, so as to assess the degree of atherosclerosis.

Conclusion : It may be concluded that measurement of carotid intima media thickness is an important tool to assess the burden of atherosclerotic complications of Diabetes Mellitus.

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Key words : DM, CAD, CPR, PAD, ABI, CIMT.

CAD is the leading cause of death in DM[1]. Diabetes is able to impair morphological and functional characteristics of the vascular wall and this condition plays as precursor of atherosclerotic disease[2]. The chronicity of DM affects many organs, systems and is responsible for the majority and mortality associated with the disease. Chronic complications can be divided into vascular and non-vascular complications. The vascular complications of DM are further divided into micro-vascular (retinopathy, neuropathy and

Editor's Comment :
- Carotid doppler is perhaps the only non-invasive method of diagnosing burden of atherosclerosis and at the same time a study regarding its correlation with ABI is simple and inexpensive method of community survey of macrovascular complications of diabetes mellitus.

nephropathy) and macro-vascular complications (CAD, cerebrovascular disease, PAD). The chronic complications usually do not become apparent until the second decade of hyperglycemia. However, since type-2 DM has a long asymptotic period of hyperglycemia, many individuals, suffering from type-2 DM have complications at the time of diagnosis.

PAD of the lower extremity is primarily the clinical manifestation of systemic atherosclerosis and atherothrombosis. With the advent of atherosclerosis, there is change in intima-media thickness(IMT) of the arterial wall along with inflammation[3]. PAD is commonly seen in type-2 DM and occurs almost three time more frequently in individuals with DM, compared to the age

and sex matched non-diabetics and it often coexists with cerebrovascular disease or coronary artery disease and therefore it is associated with poor prognosis and increased risk of morbidity and mortality[4].

Several studies have demonstrated that patients with PAD are at risk of adverse cardiovascular events compared to those individuals without PAD[5]. Coronary atherosclerosis is often clinically silent with serious morbidity or mortality as its first manifestation[6]. Patients with PAD, therefore, have an increased risk of myocardial infarction (MI), stroke and death[7,8]. The current concept of PAD is established by non-invasive tests such as, ankle-brachial index (ABI) and carotid intima-media thickness (CIMT) measurements, even before the onset of clinical symptoms[9].

Type-2 diabetes appears to confer an excess risk of cardiovascular events. Atherosclerosis is one of the primary, patho-physiological processes, underlying ischaemic cardiovascular events[10]. CIMT is strongly associated with the risk of MI and stroke in asymptomatic older adults. ABI is reliable indicator of high coronary risk and significantly related to the presence of PAD[11]. Cardiovascular risk prediction in asymptomatic individuals is mainly based on the level of cardiovascular risk factors incorporated in scoring equations. Improvement in cardiovascular risk prediction is needed and may be established by including a measure of pre-clinical atherosclerosis in the risk prediction algorithms, because atherosclerosis underlying the cardiovascular events develops over decades and has a prolonged asymptomatic phase, during which it is possible to modify the course of the disease. Measurement of CIMT has been proposed to be added to cardiovascular risk-factors to improve the individual risk assessment[12]. B-mode scan-imaging offers the ability to examine the pre-symptomatic lesion.

The patho-physiological mechanisms, by which arterial insufficiency develops, is based on the presence of arterial stenosis that progresses naturally to cause complete occlusion of the artery. Athero-sclerosis is a complex process that involves endothelial dysfunction, lipid disturbance, platelet activation, thrombosis, oxidative stress, vascular smooth muscle activation, altered matrix metabolism, remodeling and genetic factors. There is role of inflammation in all stages of development of atherosclerosis and among the bio-markers of inflammation, C-reactive protein (CRP) is associated with both the development of PAD and impaired glucose regulation. Again, the flow-distribution at the arterial bifurcation hastens the process.

AIMS AND OBJECTIVES

The study was conducted in North 24 Parganas District hospital, Barasat, so as to assess the prevalence of PAD in middle-aged (40 years and above) diabetic patients and to find out its correlation with common carotid artery intima-media thickness (CCA-IMT).

And for this to occur —

(1) ABI was measured in middle-aged diabetic patients to detect PAD.

(2) Common carotid artery intima-media thickness was measured by carotid doppler study.

(3) Correlation between CCA-IMT and PAD was done.

MATERIALS AND METHODS

A hospital-based study of seventy middle-aged (40 years and above) diabetic patients was conducted in North 24 Parganas district hospital, Barasat, Kolkata-124, from 1st April 2015 to 31st March 2016 (12 months). Patients with established CAD, patients symptomatic for PAD and patients with ABI>1.5 (because of arterial calcification with false high blood pressure) were excluded from the study. For this study, age, sex, duration of DM, systolic blood pressure of upper and lower limbs, ABI, carotid-IMT, presence of neuropathy and relevant biochemical parameters of all patients of study group were recorded.

SAMPLE SIZE WITH CALCULATION

The study was a descriptive, cross-sectional one. The number of subjects required for this study was 70.

As per study by YJV Reddy, MV Nagabhusana, Aravind Sosale, Edward. Jude, *et al* in South India on 200 rural and 400 urban patients with type-2 DM. Prevalence of ABI in type-2 DM was 17.8% ie, (p<0.01). The formulae used for sample size calculation are as follows:

Sample size in descriptive study is calculated from

$$n = \frac{(Z_{\alpha/2})^2 \times p \times q}{l^2}$$

l	-	precision in absolute term
	-	Is considered as -9
p	-	proportion from previous study
	-	is considered as -17.8%
q	=	100-p = 100-17.8 = 82.2
Z	-	normal standard deviate
$Z_{a/2}$	=	1.96 (considering 95% confidence interval, its value would be 1.96)
$(Z_{a/2})^2$	=	1.96×1.96 = 3.84

$$n = \frac{(Za/2)^2 \times p \times q}{l^2}$$

therefore,
Minimum sample size is found to be 70

STATISTICAL METHODS

Statistical analysis was performed with the help of software sas9.2, spss 15.0, stata 10.1. Using this software, basic tabulations and frequency distributions

were prepared. The mean and standard deviation were also calculated. Chi-square test was used to test the association between different study variables. Pearson correlation (r) was calculated to find the correlation between the different variables of the study. Significance level was set at 0.05, confidence interval was at 95% level. p<0.05 was considered statistically significant and CIMT were measured using doppler ultrasound Acuson X150 with 8 linear array MHz transducer and a sphygmomanometer. All measurements were performed in the supine position after 10 minutes of rest. The sphygmomanometer cuff was tied just above the elbow in arms and just above the medial malleolus in legs. The ultrasound transducer was used to locate arterial doppler signal distal to the cuff. The systolic pressure of the posterior tibial artery and brachial artery were measured bilaterally. Then for obtaining ABI highest systolic pressure of posterior tibial artery was divided by the highest systolic pressure in the brachial artery.

ABI values were interpreted as follows: abnormal (ABI=0.9), borderline (ABI 0.91-0.99), normal (1.00-1.4) or non-compressible (ABI=1.4).

Carotid intima-media thickness was carried out in common carotid artery, with the subject in supine position, neck-extended and head slightly turned to the direction opposite to the carotid artery, being examined. CIMT was measured in the far wall of common carotid artery, around 1cm below carotid bifurcation using high resolution B-Mode ultrasound machine with a linear array transducer of 8 MHz It is calculated as distance between the leading edges of lumen intima interface and media adventitia interface. Multiple measurements of ABI and CIMT were performed to improve the precision and eliminate the risk of error by measuring both the non-invasive measures.

CIMT values were recorded as: normal(<0.8mm), abnormal (>0.8mm).

Patients were divided into PAD and non-PAD groups on the basis of ABI values. Data have been analyzed accordingly and the prevalence of PAD in patients with type-2 DM were found out. Then with further statistical analysis, the correlation of PAD with carotid IMT and various other parameters of diabetes were found out.

RESULTS AND ANALYSIS

Of the total 70 cases recorded from IPD and OPD of North 24 Parganas District Hospital, Barasat were as follows:

(a) mean age-53.87 years (±8.95).

(b) mean systolic BP of lower limbs-117.17mm of Hg (±11.15).

(c) mean systolic BP of upper limbs-135.68mm of Hg (±13.93).

(d) mean ABI-0.87(±0.07).

(e) mean IMT-0.80(±0.06).

(f) 38.57% of patients were suffering from neuropathy.

(g) 25.7% of subjects were suffering from DM and hypertension.

(h) Out of 70 patients, 32 patients were less than/ equal to 50 years of age. 24 patients were 50-60 years of age. 11 patients (61-70) and only 3 patients (71-80).

(i) 51.4% of total subjects were with duration of diabetes less than/equal to 5 years. 27.1% belonged to 6-10 years of duration and subjects having DM more than 15 years were only 4.

(j) 70% of subjects were having ABI=0.9.

(k) 46% of subjects were having IMT>0.8.

(l) Out of 49 patients, having ABI=0.9, 25 patients were suffering from peripheral neuropathy and out of 21 patients having ABI >0.9, only 2 patients suffered from peripheral neuropathy. The chi-square statistics is 10.6833.p-value is .001081. The result is significant at p<0.01.

(m) Among total subjects, 74.2% (52) were non-hypertensive with 44.3% (31) subjects having ABI values =0.9. Among all subjects, 25.7% (18) were hypertensive and identified with ABI=0.9. The result is significant as the p-value is 0.001271(p<0.01).

(n) Among 46% of subjects having IMT>0.8, 21.4% subjects were hypertensive. The test is significant at chi-square statistics 13.81, p-value 0.00201(p<0.01).

(o) The chi-square statistics is 18.7538 and p-value is 0.000878 (p<0.01)- showed that most of the subjects with duration of DM more than 5 years were identified with ABI=0.9- which is significant.

(p) Out of 21 patients having ABI>0.9, only 3 patients were recorded as IMT>0.8, whereas, out of 49 patients having ABI=0.9, 29 patients were recorded as IMT>0.8. The chi-square statistics is 11.9408. The p-value is 0.000549. The result is significant at p<0.01.

(q) 92.85% (65) patients were having FBS=126mg/ dl, 84.28% (59) having PPBS=200, 18.57% (13) having low HDL and 30% (21) having high triglyceride and high LDL levels.

DISCUSSIONS

So, in this descriptive cross-sectional study, mean duration of DM was 6.76(±5.78) years with 51.4% patients were of less than 5 years duration and only 5.7% of patients belong to long duration (16-20 years).

Patients were divided into two groups : ABI (=0.9) and (>0.9). 70% among total patients were having ABI less than/equal to 0.9. 46% of total patients were identified with intima media thickness>0.8. Among these (CIMT>0.8), 41.42% subjects were having ABI=0.9. The result was highly significant as p<0.01.

The study could be compared with the study done by Pendekar S *et al*[5], where the mean age was 55.2 years (53.87 years in present study), with 68.9% cases with established CAD, proven by angiography; out of which, 64% were having abnormal ABI values, thus predicting the future risk of CAD.

The study could also be compared with Jasmine Kaur Chawla *et al*[10], which showed that type-2 DM group had higher mean CIMT as compared to the control groups. That study concluded that CIMT had association with ABI and duration of type-2 DM.

In the present study, 74.28% of all subjects were not having any other predisposing factors like hypertension; 25.71% were having hypertension with DM. Among 74.2% of non-hypertensives, 44.3% were having ABI=0.9 and 30% were having ABI>0.9. 25.7% hypertensives were identified with ABI=0.9.

61.42% of total subjects were not having peripheral neuropathy and 38.57% were having peripheral neuropathy.

Among all the patients with less 50 years of age, 11.42% were with IMT>0.8, indicating that increase in age could be correlated with increased IMT. The study also showed that there was significant correlation of IMT>0.8 with hypertension. Most of the subjects, whose duration of DM was more than 5 years, were identified with ABI=0.9. And it also showed that there was significant correlation between ABI=0.9 and IMT>0.8.

The study covered only North 24 Parganas District Hospital (Barasat) and not any other Government Hospital in the District and hence it did not reflect the true load of DM and its complications in the district. However, it suggested a way of preventing the complications of DM (viz. CAD) in a less expensive and less time-consuming way and the simple procedures could also be applied for community-based survey.

SUMMARY AND CONCLUSION

Among the total subjects, 70% of diabetic subjects were found with ABI=0.9, 30% of the subjects were with ABI>0.9. Among the 70% of diabetic subjects, 35.71% were found to be associated with peripheral neuropathy. The result is significant as the p-value is 0.001.

Among the total subjects, 46% were found with IMT>0.8mm. The result is significant as p-value is 0.0005. This indicates that ABI value=0.9 was strongly associated with increased carotid intima media thickness. The study also showed most of the diabetic subjects with age 40 years and above have abnormal ABI and an associated increased CIMT.'

Subjects with increased CIMT had increased risk of atherosclerotic complications.

Thus, it may be concluded that measurement of carotid intima media thickness is a simple, inexpensive, time-saving procedure that may be used to measure the degree of atherosclerotic burden and complications of diabetes mellitus.

LIMITATIONS

The study is Institution (District Hospital) based – and so the sample size is small; as a result, some data may be exaggerated or there may be under-reporting.

REFERENCES

1 Bafgi SMHS, Ratki SKR, Bafgi SAS, Razavi SH, Mardanshahi A, Namiranian N, *et al* — The association of carotid Intima-media thickness and ankle brachial index with SPECT myocardial perfusion imaging in asymptomatic diabetic patients. *Iranian Journal of Diabetes and Obesity* 2015; **7(4)**.

2 Roever L, Peo Reis — Screening for peripheral arterial disease: An update. Roever and Reis. *J Vasc Med Surg* 2015; **3(3)**.

3 Amer MS, Rahman A A, Gawad WMAE, Aal IAA, Mohamed A AKAR, Wahab WEHMA — Relationship between peripheral arterial disease, carotid intima-media thickness and c-reactive protein in elderly diabetic patients 2013; **2(4):** 115-20.

4 Pradeepa R, Chella S, Surendar J, Indulekha K, Anjana RM, Mohan V — Prevalence of peripheral vascular disease and its association with carotid intima-media thickness and arterial stiffness in type 2 diabetes; the Chennai urban rural epidemiology study (CURES III). Diabetes& Vascular Research I-II.2014.

5 Pendekar S, Singh N, James E, Pandey D — Ankle brachial index as a predictor of coronary artery disease in diabetic patients. IAIM 2016; **3(4):** 91-6.

6 Meenakshisundaram R, Devidutta S, Michaels AD, Senthilkumaran S, Rajendiran C, Thirumalaikolundu subramanian P — Significance of the intima-media thickness of the carotid and thoracic aorta in coronary artery disease in south Indian population. *Heart Views* 2011 Oct-Dec; **12(4):** 150-6.

7 Thiruvoipati T, Kielhorn CE, Armstrong EJ — Peripheral artery disease in patients with diabetes: epidemiology, mechanisms, and outcomes. *World J Diabetes* 2015 July 10; **6(7):** 961-9.

8 Sarangi S, Srikant B, Rao DV, Joshi L, Usha G — Correlation between peripheral arterial disease and coronary artery disease using ankle brachial index- a study in Indian population. *Indian Heart J* 2012 Jan; **64(1):** 2-6.

9 Brasileiro ACL, Oliveira DCD, Victor EG, Danielle AG, Oliveira C, Batista LL — Association between ankle brachial index and carotid atherosclerotic disease. *Arq Bras Cardiol* 2013; **100(5):** 422-8.

10 Chawla KJ, Shenoy S, Sandhu JS — Association of carotid artery intima media thickness with traditional risk factors of atherosclerosis in patients with type 2 diabetes mellitus and hypertension. *International Journal of Science and Research* 2014 May; **3(5)**.

11 Patil DR, Nikumbh SD, Roplekar K, Parulekar A — Anterior wall myocardial infarction with special reference to carotid intima-media thickness, ankle brachial pressure index, and echocardiographic evaluation. *International Journal of Scientific Study* 2014 August; **3(5)**.

12 Ruijter IMD, Peters SAE, Anderson TJ, Dekkar JM, Eijkemans MJ, Engstrom G, *et al* — Common carotid intima-media thickness measurement in cardiovascular risk prediction a meta analysis. *JAMA* 2012; **308(8):** 796-803.